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CONTENTS

PRE-TRANSFUSION TESTING FOR THE CHRONICALLY TRANSFUSED, SENSITIZED PATIENT: A SIMPLE, TIME-SAVING APPROACH

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Introduction

A recent California Blood Bank Society panel discussion of how often repeat testing should be done for chronically transfused, sensitized patients prompted a survey, the results of which are the subject of this paper.

With the advent of the diagnosis-related groups (DRGs), some blood banks have been forced to lower their rates for reimbursement for serologic testing. This has led to decreased income, and in some cases a decrease in staffing. However, blood bankers are committed to high-quality patient care and safe transfusions and are trying to find more efficient and economical methods for pre-transfusion testing on the chronically transfused, sensitized patient. The serologic workup for these patients always requires more time, and we need more efficient ways to handle their transfusions without compromising quality.

A survey of the regulatory agencies revealed that there are no guidelines to determine the standards of practice. The Food and Drug Administration is concerned with licensing establishments and products, manufacturing practices, biological product standards, standards of blood products, and standards of diagnostic reagents. It makes no recommendations about testing protocols.[1]

The state of California (California Administrative Code) is concerned with licensing laboratories and individuals, and with training schools, clinical laboratory standards, proficiency tests, and laboratory reports. It makes no recommendations about testing protocols.[2]

Finally, the American Association of Blood Banks (AABB) publishes the *Standards for Blood Banks and Tranfusion Services,* which does not include recommendations about how often to repeat the testing on chronically transfused, sensitized patients. It recommends screening recipients' blood for unexpected antibodies, but there is no advice as to how frequently antibody identification should be repeated.[3]

The goal of repeated antibody identification is easy to define. It is to determine whether the patient has made any new clinically significant antibodies. The answers to "How often should we test?" and "To what extent should we test?" are elusive. Since there are no specific regulations or recommendations, a survey of transfusion service laboratories and blood banks was made to determine the standards of practice.

Materials and Methods

A survey was sent to 167 transfusion service laboratories and donor centers in the state of California, and 142 (85%) responded. Of the institutions surveyed, 14 were donor centers and 128 were hospitals. The

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donor centers are blood collecting facilities that do not crossmatch blood; however, they offer reference laboratory and consultation services to hospitals. The data were subdivided in several ways, ie, large hospitals (>300 beds) vs small hospitals (<300 beds), and northern California hospitals vs southern California hospitals—using Fresno, California, as an arbitrary dividing point between northern and southern California. This was done to compare the transfusion practice in different sized hospitals and to look for regional differences in transfusion practice. The percentages in the tables of data were calculated by dividing the number of responses to an item by the total number of surveys (142) and multiplying by 100. In some cases the percentages per item may total more than 100%, and in other cases they may total less than 100%. This occurred when people responded to more than one choice, or when they failed to respond to any of the choices. The results of the survey follow.

Results

Subject: pretransfusion testing on chronically transfused, sensitized patients.

1. Do you repeat ABO and Rh typing? If yes, on every specimen or periodically?

	Total	Donor Centers	Hosp. <300 beds	Hosp. >300 beds	Hosp. No. CA.	Hosp. So. CA.
	$n=142$	$n=14$	$n=55$	$n=73$	$n=58$	$n=70$
No	<1%	0	0	3%	0	3%
Yes	98%	93%	100%	97%	100%	97%
Every specimen	96%	93%	96%	97%	98%	95%
Periodically	<1%	0	2%	0	0	2%

2. Do you repeat the antibody screen?
   _____ No, we proceed directly to a panel if the patient is known to be sensitized
   _____ Yes, on every specimen
   _____ Yes, unless all screening cells are expected to be positive

	Total	Donor Centers	Hosp. <300 beds	Hosp. >300 beds	Hosp. No. CA.	Hosp. So. CA.
	$n=142$	$n=14$	$n=55$	$n=73$	$n=58$	$n=70$
No	21%	50%	22%	13%	10%	23%
Yes, every*	56%	36%	74%	46%	47%	67%
Yes, unless	10%	14%	4%	13%	6%	12%

*Nine institutions reported using selected cells

No. CA. < 300 beds	1
No. CA. > 300 beds	2
No. CA. Donor Center	1
So. CA. <300 beds	3
So. CA. >300 beds	2

3. Do you repeat the autocontrol as part of the pretransfusion testing?

	Total	Donor Centers	Hosp. <300 beds	Hosp. >300 beds	Hosp. No. CA.	Hosp. So. CA.
	$n=142$	$n=14$	$n=55$	$n=73$	$n=58$	$n=70$
No	23%	14%	14%	31%	12%	33%
Yes	75%	79%	82%	69%	84%	67%

4. Do you repeat the direct antiglobulin test (DAT) as part of pre-transfusion testing?
   _____ No
   _____ No, but we do the autocontrol
   _____ Yes

	Total	Donor Centers	Hosp. <300 beds	Hosp. >300 beds	Hosp. No. CA.	Hosp. So. CA.
	$n=142$	$n=14$	$n=55$	$n=73$	$n=58$	$n=70$
No	21%	0	18%	27%	14%	30%
No, auto	56%	43%	66%	51%	63%	53%
Yes	24%	50%	18%	22%	24%	18%

5. How often do you repeat antibody identification on known sensitized patients?
   _____ Every specimen
   _____ Every readmission to the hospital
   _____ Periodically, specify _____
   _____ When reactions (rx) appear stronger
   _____ When antibody screening cells or donor cells are unexpectedly positive

	Total	Donor Centers	Hosp. <300 beds	Hosp. >300 beds	Hosp. No. CA.	Hosp. So. CA.
	$n=142$	$n=14$	$n=55$	$n=73$	$n=58$	$n=70$
Every specimen	27%	14%	36%	22%	27%	29%
Every readmission	27%	36%	30%	24%	29%	24%
Periodically increased rx	20%	0	20%	24%	20%	24%
Unexpected rx	54%	50%	48%	60%	57%	53%

	Donor Centers	Hosp. <300 beds	Hosp. >300 beds	Hosp. No. CA.	Hosp. So. CA.
Every specimen	1	1	9	2	15
48 hours	1	5	4	2	9
72 hours	0	0	1	0	2
5 days	0	1	2	5	0
Weekly	0	2	6	5	5
10 days	0	1	1	0	3
2 weeks	0	0	3	0	6
3 weeks	0	0	1	0	2
Monthly	0	1	3	1	5
3 months	1	0	4	4	0
4 months	0	1	0	1	0
Annually	0	0	1	1	0

6. If the patient has a chronically positive (IgG) DAT, how often do you perform an elution?
   _____ Every specimen
   _____ Only if transfused in the past three months
   _____ Periodically, specify _____
   _____ Not if a previous specimen yielded a non-reactive or non-specific eluate
   _____ When the DAT is <1+
   _____ When the DAT is 1+ or greater

	Total	Donor Centers	Hosp. <300 beds	Hosp. >300 beds	Hosp. No. CA.	Hosp. So. CA.
	$n=142$	$n=14$	$n=55$	$n=73$	$n=58$	$n=70$
Every specimen	12%	7%	18%	9%	16%	11%
Transfused in past 3 months	47%	50%	42%	49%	43%	48%
Periodically, previously nonreactive/nonspecific	23%	21%	16%	28%	25%	21%
DAT <1+	2%	7%	2%	1%	0	3%
DAT 1+	17%	7%	22%	15%	25%	12%

	Donor Centers	Hosp. <300 beds	Hosp. >300 beds	Hosp. No. CA.	Hosp. So. CA.
Increased DAT	5	5	14	7	12
Decreased hemoglobin	2	4	5	5	4
On admission	1	1	1	1	1
48 hours			1		1
2–4 days			2	1	1
1–2 weeks		1	1	1	1
14 days		1	1		2
4 weeks			1		1
Do not do elutions		4		2	2

7. In a non-emergency situation, if antigen-negative donor units appear compatible by crossmatch, would you delay transfusion until antibody identification was completed?

	Total	Donor Centers	Hosp. <300 beds	Hosp. >300 beds	Hosp. No. CA.	Hosp. So. CA.
	$n=142$	$n=14$	$n=55$	$n=73$	$n=58$	$n=70$
Yes	79%	93%	76%	79%	71%	83%
No	17%	0	18%	19%	27%	12%

Discussion

Although no attempt was made to analyze the data statistically, certain observations can be made about each question (listed here by question number).

1. Almost all institutions repeat the ABO and Rh typing on every specimen. A report from one indicates that a forward and reverse ABO grouping is performed on the first specimen from a patient; however, only a reverse grouping is performed on subsequent specimens. This would satisfy the need to confirm the identity of the specimen while reducing the workload and the volume of commercial antisera used.
2. Fifty-six percent of the institutions indicate that the antibody screening test is repeated on every specimen. Selected cells are used in some laboratories while others immediately test a panel of cells. This is an area where efficiency may be increased. It is interesting to note that 74% of hospitals with fewer than 300 beds repeat the antibody screening test on every specimen.

3 & 4. An autocontrol is included as part of the pre-transfusion testing in a majority of institutions; however, only 24% repeat the DAT as part of pre-transfusion testing.

5. When to repeat antibody identification is an area that shows a complete lack of consensus in this survey. Even those institutions that indicate they repeat the antibody identification "periodically" lacked consensus about how often "periodically" means.

   It is surprising that 100% of the institutions do not repeat the antibody identification when reactions appear stronger or when antibody screening cells or donor cells are unexpectedly positive. These are both indications of new sensitization.

6. There is no clear consensus about how often to repeat an elution if a patient had a chronically positive DAT. Perhaps the most significant point is that elution is not repeated in 47% of the institutes surveyed unless the patient had been transfused in the past three months. Since transfused red cells do not persist in significant numbers after three months, a positive DAT at that point would represent autoantibody or be due to drugs.
7. In a non-emergency situation, a majority of institutions indicated that an antibody identification would be completed before transfusing the patient. The crossmatch would not be relied on to find compatible units. Since weakly reacting antibodies may show dosage and only react with red cells having a homozygous expression of the antigen, the crossmatch is not always a safe alternative to antibody identification.

Comment

The following suggestions are neither new nor original, but are simple and time-saving. They increase laboratory efficiency in antibody detection and identification while maintaining safe transfusion practice.

A. When a patient first becomes a candidate for transfusion, identify all antibodies in the serum.
B. Select methods for antibody detection that avoid known clinically insignificant antibodies.
   1. Cold autoagglutinins

a. Prewarmed technique
b. Saline media
c. Using patient's plasma instead of serum (reduces in vitro complement binding)
d. Anti-IgG antiglobulin reagent

2. Rouleaux
   a. Saline dispersal
   b. Saline replacement
3. Neutralization
   a. Anti-P_1: commercial substance or hydatid cyst fluid
   b. Anti-Le: commercial substance or saliva
   c. Anti-Sd^a: urine
   d. Anti-Ch^a, anti-Rg^a: serum/plasma

C. Use time-saving approaches to identify clinically significant antibodies in sensitized patients.[5]
1. Phenotype
   a. Recommended typings include:
      (1) Rh: D, C, E, c (plus e if E+)
      (2) Kell: K (plus k if K+)
      (3) Duffy: Fy^a, Fy^b
      (4) Kidd: Jk^a, Jk^b
      (5) MNSs: S, s
   b. Red cell separation may be necessary to determine the accurate phenotype if the patient has been recently transfused.[4]
2. Select cells for antibody identification.
   a. Using the patient's phenotype, select panel cells with a homozygous expression of the antigens the patient lacks.
   b. If the patient appears to have an antibody to a high incidence antigen, it is essential to phenotype the red cells with appropriate reagents. Periodic testing with selected cells lacking the high incidence antigen should be done to look for new underlying antibodies.
3. Reconfirm previously identified antibodies using a reagent red cell with a heterozygous expression of the antigen.

   It is not necessary to reconfirm the presence of known, clinically significant antibodies with reagent red cell panel studies; however, it may be time-saving and economical to include a known positive reagent red cell of heterozygous antigen expression along with donor units being crossmatched. If the reagent red cell with heterozygous antigen expression is positive with the patient's serum, crossmatch-compatible units may be considered antigen-negative; thus eliminating the need to type the donor units with commercial antiserum (see AABB Std. G4.110).[3]

References:

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COLD AUTOIMMUNE HEMOLYTIC ANEMIA WITH AUTO-ANTI-AI SPECIFICITY: ^{51}CHROMIUM SURVIVAL STUDIES

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Abstract

A 65-year-old woman was found to have severe autoimmune hemolytic anemia. The patient was group A_1, $Rh_o(D)$ positive. The direct antiglobulin test was strongly positive with anti-C3 and negative with anti-IgG. The serum contained two distinct IgM antibodies, auto-anti-I and auto-anti-AI. Both were reactive at 22°C. However, the anti-AI also was reactive in saline and in albumin at 37°C. An eluate revealed anti-AI and a weak anti-I. Sequential ^{51}Chromium survival studies were done with group OI and AI red cells. The group OI red cells survived normally (97% at 24 hours) while the group A_1I red cells were removed in a "two-component" pattern characteristic of IgM complement-fixing antibodies (62% survival at one hour, 49% at 24 hours). Based on these observations, the patient was subsequently transfused without incidence with six group O units of washed red cells prior to splenectomy. Although auto-anti-AI has been previously reported, this is the first case to demonstrate the use of ^{51}Cr survival studies to determine its clinical significance.

Introduction

Cold reactive red cell autoantibodies are frequently detected at temperatures below 22°C. These cold reactive antibodies are of little clinical significance and are usually disregarded for transfusion purposes.[1]

On occasion, cold autoantibodies display an unusually wide thermal range of reactivity that results in detection at physiologic temperatures. The clinical importance of these antibodies cannot be easily determined unless careful clinical and serological assessment of individual cases is undertaken.

We present a case in which differential serological testing and ^{51}Cr survival studies determined the transfusion protocol for a patient with auto-anti-AI in her serum.